REMARKS/ARGUMENTS

I. Status of the Claims.

Claims 36-96 are pending. Claims 44-65 and 74-96 have been withdrawn from examination by the Examiner as being directed to non-elected subject matter. Claims 36-43 and 66-73 are under examination. By this Response, no new matter has been added to the application.

II. Claim Rejections.

Pending claim rejections are summarized and addressed as follows.

(i) Double patenting. Claims 36-43 and 66-73 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over certain claims of co-pending application no. 10/001,245 ("the '245 application"). Applicants confirm that the '245 application has not issued as a patent. Accordingly, Applicants are not required to respond to the instant rejection at this time.

It is noted that the instant application was filed prior to the '245 application. Thus, according to the rules of practice, if the obviousness-type double patenting rejection is the last remaining rejection in the instant application and rejections remain in the '245 application, the obviousness-type double patenting rejection of the instant claims should be withdrawn and the application permitted to issue as a patent without the filing of a terminal disclaimer. *See* MPEP §804.I.B.1.

(ii) Rejection Under 35 U.S.C. §112, first paragraph (written description).

Claims 36, 38-43 and 66-73 remain rejected for alleged failure to comply with the written description requirement. The Examiner maintains the specification fails to provide adequate written description for the functional limitations set out in the claims. The rejection is respectfully traversed on the grounds that the specification and claims describe the claimed invention in language that is readily understood by one of ordinary skill in the art and the

claimed genus of recombinant Bet v 1-related mutant allergens share a level of homology that serve as the common structural feature for the functional language recited in the claims.

Applicants' previously-filed amendments and responses have outlined in detail the reasons why the specification provides written description for the claimed invention. *See*, e.g., responses filed April 30, 2008 and February 6, 2009.

Thus, it was general knowledge in the art at the time the application was filed that allergens with reduced IgE binding could be produced by site-directed mutagenesis. *See* specification and cited references at page 7, line 26, et seq. The specification further discloses that the amino acids available for antibody binding are located on the surface of allergens (*see* specification at page 19, lines 30-36). The functional characteristic of reduced IgE binding flows directly from (i.e., is "coupled with") the known property of IgE epitopes to be present on the surface of allergens, particularly in conserved patches on the allergen surface, and the disclosed and well known correlation that disrupting IgE epitopes will reduce IgE binding. The state of the art was such that it was known, for example, that Bet v 1 allergens include IgE epitopes, that they reside in surface patches, that Bet v 1 proteins from the order Fagales share a high level of identity and exhibit cross reactivity, and that substitution of amino acids on the surface of Bet v 1 allergens could disrupt IgE epitopes and lower IgE binding.

The specification sets forth that:

> The major birch pollen allergen Bet v 1 (SEQ ID NO: 37) shows about 90% amino acid sequence identity with major allergens from pollens of taxonomically related trees, i.e. *Fagales* (or instance hazel and hornbeam) and birch pollen allergic patients often show clinical symptoms of allergic cross-reactivity towards these Bet v 1 homologous proteins.

Specification at page 24, lines 8-14. Based on the level of skill in the art at the time the application was filed, a worker of ordinary skill in the art would have recognized that the high degree of identity among Bet v 1 homologous proteins from the order Fagales and the finding

that birch pollen allergic patients exhibited symptoms of allergic cross-reactivity towards these homologous proteins indicates that Bet v 1 homologous proteins from the order Fagales have highly similar primary sequences and three-dimensional structures, indicating that the features that are set forth above and which indicate that the Applicants had possession of the mutant allergens for Bet v 1 proteins from the order Fagales also hold for the broader genus of recombinant mutant allergens of Bet v 1 homologous proteins from the order Fagales. Thus, the specification provides written description for the full scope of recombinant mutant Bet v 1 allergens from the order Fagales. *See* claims 36 and 66.

The specification read in light of the knowledge of the state of the art also provides written description for each of the particular features recited the claims. Thus, the general level of skill and knowledge in the art would readily allow one of ordinary skill in the art to use the known crystal structure of Bet v 1 and/or sequence alignment of Bet v 1 sequences to identify amino acids that have a solvent accessibility of 20% (claims 38 and 68), identify amino acids that are conserved with 70% identity among Bet v 1 allergens from the order Fagales (claims 39 and 69), wherein a conserved solvent-accessible amino acid residue is within a patch of conserved amino acid residues connected over at least 400Å of the surface of said naturally-occurring Bet v 1 allergen (claims 42 and 72), wherein the solvent-accessible amino acid residue that is conserved among Bet v 1 homologous allergens within the taxonomic order from which said naturally-occurring Bet v 1 allergen is substituted with an amino acid that is not conserved among Bet v 1 homologous allergens within the taxonomic order from which said naturally-occurring Bet v 1 allergen occurs (claims 43 and 73) and wherein said allergens homologous to Bet v 1 have an amino sequence that yields a BLAST probability of less than 0.1 when compared to an amino acid sequence of SEQ ID NO: 37 (claim 67). The specification further provides extensive guidance on tests that can be used to determine with recombinant Bet v 1 allergens have IgE binding reduced by at least 5%, compared to the naturally-occurring Bet v 1 allergen from which it is derived (claims 40 and 70) and wherein average root mean square deviation of the atomic coordinates comparing the α-carbon backbone tertiary structures of said recombinant

mutant Bet v 1 allergen and said naturally-occurring Bet v 1 allergen is less than 2Å (claims 41 and 71).

Thus, the Applicants were in possession of the complete subject matter of claims 36, 38-43 and 66-72.

In short, the structure of Bet v 1 was known at the time the application was filed and Bet v 1 allergens are highly conserved. There is no rule that the Applicants provide description of the precise mutant amino acids in the claimed recombinant Bet v 1 mutants. *Falkner v. Inglis,* 448 F.3d 1357, 1366 (Fed. Cir. 2006). Applicants are entitled to "flexibility" in how they claim their invention. *Univ. of Rochester v. G.D. Searle & Co., Inc.,* 358 F.3d 916, 927-928 (Fed. Cir. 2004). In *Ariad v. Eli Lilly*, the Federal Circuit reiterated, "[written description] doctrine never created a heightened requirement to provide a nucleotide-by-nucleotide recitation of the entire genus of claimed genetic material; it has always expressly permitted the disclosure of structural features common to the members of the genus." *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.,* cv 2008-1248, Fed. Cir., *en banc,* decided March 22, 2010, slip op at 26, *citations omitted.* Here, the claims call for "a substitution of a solvent-accessible amino acid residue that is conserved among *Bet v 1* homologous allergens within the taxonomic order *Fagales*, said substitution occurring in a B-cell epitope of said naturally-occurring *Bet v 1* allergen" (*see* claim 36) or "a substitution of a solvent-accessible amino acid residue that is conserved among homologous allergens within the taxonomic order *Fagales*, said substitution occurring in a B-cell epitope of said naturally-occurring allergen" (*see* claim 66), where the substitution leads to reduced IgE binding. When measured against the known, conserved structure of Bet v 1 allergens and the high level of skill in the art concerning B-cell epitopes, the claims tell one of ordinary skill in the art where mutations are placed in the claimed recombinant allergens. The claims thus describe the claimed invention and do not "merely [draw] a fence around the outer limits of a purported genus." *Id.* at 21.

For at least the reasons set forth above, the specification provides sufficient written description to show Applicants were in possession of the full scope of the claimed

invention when the application was filed. Reconsideration of the claims and withdrawal of all rejections thereof for lack of written description is requested.

III. Conclusion.

This application is believed to be in condition for allowance.

Respectfully submitted,

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